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EXAMINER	
KIM, ALEXANDER D	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,064	DEMMER ET AL.	
	Examiner	Art Unit	
	ALEXANDER D. KIM	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-7 and 9-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-7 and 9-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. In response to the previous Office action, a non-Final rejection (mailed on 04/29/2008), Applicants filed a response and amendment received on 07/28/2008. Said amendment cancelled Claims 2-3, 8 and 16; amended Claims 1, 9, 13 and 15.

Claims 1, 4-7, 9-15 are pending in the instant Office action and will be examined herein.

Withdrawn-Objections to the Specification

2. The previous objection to the specification because the title is not descriptive of the claims is withdrawn by virtue of Applicants' title amendment (filed on 7/28/2008).

3. The previous objection to the specification because the Abstract is missing, is withdrawn by virtue of filing the Abstract.

Claim Objections

4. The previous objection to Claim 1 because the use of abbreviation "Da" is withdrawn by virtue of Applicants' amendment.

5. The previous objection to Claim 13 because the use of abbreviation "DEAE, DEA, CM, QA, TMA, S, SP" is withdrawn by virtue of Applicants' amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

6. Claim 13 is rejected under 35 U.S.C. 112, first paragraph, **new matter**, as failing to comply with the written description requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Instant rejection is necessitated by the claim amendment.

Claim 13 recites "diethyl aminoethyl", "2,2'-iminodiethanol", "carboxymethyl, N,N-diethyl-N-(2-hydroxy-1-propyl)-ammoniethyl", "trimethylamine", "sulfonylmethyl", and "sulfopropyl"; which limitations are not supported by the original disclosure. The applicant is advised to point out the support in the original disclosure or amend the instant claims.

7. Claims 1, 4-7 and 9-15 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was stated in the previous office action as it applied to previous Claims 1 and 3-15. In response to this rejection, applicants have cancelled Claims 2-3, 8 and 16; amended Claims 1, 9, 13 and 15; and traverse the rejection as it applies to the newly amended claims.

Applicants argue that instant rejection is moot in view of instant amendment; wherein the amendment are drawn to a method for purifying and/or isolating filamentous bacteriophages using a metal ion containing membrane; wherein the metal ion containing membrane are broadly described in the specification.

Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. The examiner acknowledges that instant claims are amended to a method of purifying filamentous bacteriophages. However, the claims are still drawn to a genus of method involving an affinity chromatography by loading any filamentous bacteriophages to any metal ion containing membrane which does not satisfy the written description requirement; wherein the term "filamentous bacteriophage "is disclosed as a very widely varying genus bacteriophage having a helical symmetry (see bottom of page 5, for example) as long as it has molecular weight of greater than $1x10^6$ Da using any affinity chromatography having any membrane (containing a metal ions) made up of any materials.

As previously noted, the instant specification teach a method for purifying and/or isolating high-molecular compounds contained in a solution or a suspension with the capacity for metal chelate formation, the method comprising the steps of: (a) applying a solution or suspension containing the high-molecular compounds bacteriophage M13

onto the Sartobind® Membrane with imidodiacetic acid (IDA) type 19442 with Cu2+ ions; and (b) separating the bacteriophage M13 by Sartobind® Membrane (with imidodiacetic acid attached as binding entity or functional group). The breadth of claim includes a method step involving a solution of any filamentous bacteriophage as long as it has molecular weight of greater than $1x10^6$ Da; and/or involving any affinity chromatography having any membrane (containing metal ions) made up of any materials. The prior art do not teach a representative species of claimed method. The specification discloses one method described above using Sartobind® Membrane with imidodiacetic acid (IDA) type 19442, which is encompassed by the breadth of Claims 1 and 3-15. However, the prior art and the instant specification do not describe the claimed genus method as disclosed in the breadth of claims above comprising purification of any high molecular compound, and/or steps involving any metal ion affinity chromatography with any membrane (containing metal ions) made up of any material. Also, the claimed method in Claim 1 is not limited to the use of particular affinity chromatography (that is the affinity are created by the metal chelating property of membrane and the high molecular compounds) as long as the membrane used in chromatography contains a metal (e.g., metal ions from a buffer). A method of instant specification and prior arts do not describe a genus method, as described in the breadth of claims, sufficiently to represent the correlation between the structures of any high molecular compound, any affinity membrane used in steps and function of purifying any high molecular compound having molecular weight greater than $1x10^6$ Da. Thus the instant specification and the prior art cannot describe the structure of a very broad

claimed genus and one skilled in the art would not be in possession of the claimed genus by the instant specification.

8. Claims 1, 4-7 and 9-15 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement, because the specification, while being enabling for method comprising the steps of applying a solution or suspension containing the bacteriophage M13 onto the Sartobind® Membrane Adsobers with an imidodiacetic acid (IDA) type 19442 charged with Cu^{2+} ions and separating the bacteriophage M13; does not reasonably provide enablement for a method step involving a solution of any filamentous bacteriophages as long as it has molecular weight of greater than $1x10^6$ Da; and/or involving any affinity chromatography having any membrane (in the presence of a metal ions) made up of any materials.

The rejection was stated in the previous office action as it applied to previous Claims 1 and 3-15. In response to this rejection, applicants have cancelled Claims 2-3, 8 and 16; amended Claims 1, 9, 13 and 15; and traverse the rejection as it applies to the newly amended claims.

Applicants argue that instant rejection is moot in view of instant amendment; wherein the amendment are drawn to a method for purifying and/or isolating filamentous bacteriophages using a metal ion containing membrane; wherein the metal ion containing membrane are broadly described in the specification.

Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. The examiner acknowledges that instant claims

are amended to a method of purifying filamentous bacteriophages. However, the claims are still drawn to a genus of method involving an affinity chromatography by loading any filamentous bacteriophage to any metal ion containing membrane which does not enables full scope of claimed invention; wherein the term "filamentous bacteriophage" is disclosed as a very widely varying genus bacteriophage having a helical symmetry (see bottom of page 5, for example) as long as it has molecular weight of greater than $1x10^6$ Da using any affinity chromatography having any membrane (containing a metal ions) made up of any materials.

The specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use of the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of

experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The nature of the invention is drawn to a method for purifying and/or isolating high-molecular compounds contained in a solution or a suspension with the capacity for metal chelate formation, the method comprising the steps of: (a) applying a solution or suspension containing the high-molecular compounds bacteriophage M13 onto the Sartobind® Membrane with imidodiacetic acid (IDA) type 19442 charged with Cu^{2+} ions; and (b) separating the bacteriophage M13. The breadth of claim includes a method step involving a solution of any filamentous bacteriophage as long as it has molecular weight of greater than $1x10^6$ Da; and/or involving an affinity chromatography by any membrane (containing metal ions) made up of any materials. Applicants teach a method of purifying M13 bacteriophage using a commercially available Sartobind® Membrane with imidodiacetic acid (IDA) type 19442 with Cu^{2+} ions. The prior art does not teach no direction or guidance for purifying any filamentous bacteriophage using any membrane containing membrane. Thus, applicants and prior arts disclose no direction or guidance on how to make and use any other representative species for claimed genus method that is a method comprising step of using any affinity chromatography having any membrane containing metal ions for purifying any filamentous bacteriophages as long as the molecular weight is greater than $1x10^6$ Da.

Thus, the specification and prior art fail to describe how to make and use the claimed genus method sufficiently. Therefore, it is unpredictable for claimed genus method to be used in the method of purifying any filamentous bacteriophages (i.e., MW of more than $1x10^6$ Da). It is unpredictable to purify any filamentous bacteriophages purification by purification method encompassed by the breadth of claims for one skilled in the art to make and use the full scope of claims. The said unpredictability makes the relative skill required in the art very high. For all of the above reason, it would require undue experimentation necessary for the claimed method for purifying any high-molecular compounds.

Withdrawn-Claim Rejections - 35 USC § 103

9. The previous rejection of Claims 1 and 3-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sartobind® Membrane Adsorbers brochure-A (2003, see the attachment) as evidenced by Fischer-Fruhholz (May 16, 2003, Applications Membrane Adsorbers) and Stevely (Journal of Virology, 1977, volume 22, pages 232-234), and in view of Sartobind® Membrane Adsorbers brochure by Hirai et al. (29, Sept 2003, Virus Purification and Removal with Sartobind® Membrane Adsorbers, see the attachment) is withdrawn by virtue of Applicants amendment (i.e., reciting the limitation of filamentous bacteriophages).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1, 4-7 and 9-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sartobind® Membrane Adsorbers brochure-A (2003, see the attachment, as previously cited) in view of Fischer-Fruhholz (May 16, 2003, Applications Membrane Adsorbers, see the attachment, as cited previously), Sartobind® Membrane Adsorbers brochure by Hirai et al. (29, Sept 2003, Virus Purification and Removal with Sartobind® Membrane Adsorbers, see the attachment, as cited previously) and Rudgers et al. (Protein Engineering, 2001, volume 14, pages 487-492) as evidenced by Hondel et al. (Eur. J. biochem., Volume 68, pages 55-70). Instant rejection is necessitated by the claim amendments.

The rejection was stated similarly in the previous office action as it applied to previous Claims 1 and 3-15. In response to this rejection, applicants have cancelled Claims 2-3, 8 and 16; amended Claims 1, 9, 13 and 15; and traverse the rejection as it applies to the newly amended claims.

Applicants traverse instant rejection because Fischer-Fruhholz does not teach or suggest the use of metal ions containing membranes for virus purification; and Stevely's invention is remote and relates to isolation of viral DNA and electron microscopic examination of the DNA. Applicants argue that Hirai does not teach or suggest the use of metal ions containing membranes for virus purification. Applicants argue that the "Sartobind® Membrane Absorbers brochure-A" nowhere describes or suggests the use

of metal ions containing membranes for use in virus purification. Applicants argue that the purification of viruses results in a surprisingly high yield and surprisingly high purity of the virus as well as in a surprisingly large amount of purified material per surface unit of the membrane as shown on paragraph "[0022]", "[0023]" and "[0025]"; thus, the unexpected advantages of the presently claimed method of the present invention are not described or suggested in any references.

Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. As previously noted, "Sartobind® Membrane Absorbers brochure-A" teaches a method of purifying a "virus", which is specifically recited under the "Application", on page 5; wherein the Sartobind® Membrane Absorber includes a metal ion chelating membrane as evidenced by Fischer-Fruhholz (see page 5). As applicants acknowledged, the "Sartobind® Membrane Absorbers brochure-A" as well as Fischer-Fruhholz is a general overview of various types of membranes, including metal chelate membranes; and the applications for such membranes includes virus purification; thus, suggesting and providing motivation to use Sartobind® Membrane Absorbers for virus purification and/or removal from a sample. Thus, Fischer-Fruhholz et al. teach the general "Applications Membrane Adsorbers" (see Title) including the metal chelating affinity chromatography on page 5 and the removal of virus by binding the virus to the membrane on pages 32-34 (although, Q anion exchanger membrane is used as a specific example). Because one skilled in the art recognize that a virus having a coat protein would bind to a ion chelating membrane and be isolated or removed by the membrane, as long as the coat protein of the virus is capable of binding

to metal chelating membrane. The binding of virus to an affinity membrane depends on the coat protein regardless of the virus is filamentous or not; thus, one skilled in the art knows that Sartobind® Membrane Absorbers having metal chelating binding group can be used to purify any virus including but not limited to any filamentous virus. Furthermore, Fischer-Fruhholz teach that the metal chelate affinity membrane have "affinity to His, Cys, Trp present in almost every protein" (see page 5 of Fischer-Fruhholz) wherein said every protein can be a part of coat protein in any filamentous bacteriophages.

Regarding the surprising results as alleged by applicants by reciting the paragraphs "[0022]", "[0023]" and "[0025]", assuming these paragraphs is referring to a USPAP, the examiner does not find any surprising and unexpected results because said paragraphs only describe preferred embodiment of the instant application.

Sartobind® Membrane Adsorbers brochure-A teach a method of purification using "Sartobind MultiSep Membrane Adsorbers" which is used in chromatography as shown in the figures on page 5, wherein the membrane type includes "Sartobind IDA (iminodiacetic acid) metal chelate", wherein the applications includes "Viral purification" (see middle, under the Application on page 6). Thus, Sartobind® Membrane Adsorbers brochure teach a step of applying a solution containing high molecular biopolymers as exemplified by the graph showing the UV detection vs. flow rate of a column chromatography (see page 2) and separating virus as indicated under "Applications" (see page 6, middle); and meets the limitation of claim 1, 3 and 8 except that the virus is filamentous virus with a molecular weight of $1x10^6$. The Sartobind® Membrane

Adsorbers is made of "cellulose" (see top of page 1) and have pore size of "3-5 um" (see top of page 4), which meets the limitation of claims 6-7.

Sartobind® Membrane Adsorbers with Cu^{2+} is evidenced by the teaching of charging with Cu^{2+} as evidenced by Fischer-Fruhholz (see page 5); thus, meeting the limitation of claims 4-5.

Sartobind® Membrane Adsorbers brochure by Hirai et al. teach that the Sartobind® Membrane Adsorbers is used to purify a virus including "pseudorabies virus (PrV)" on page 32, wherein the PrV has molecular weight greater than $1x10^6$ because "The whole native DNA has a molecular weight of $90x10^6$ to $95x10^6$" (see Abstract of Stevely).

Sartobind® Membrane Adsorbers brochure-A does not teach a method for purifying a filamentous virus having $1x\ 10^6$ daltons and with additional method step of additional ion exchange chromatography prior to step (a) of Claim 1, or additional filtration for the removal of additional impurities.

Rudgers et al. teach a filamentous bacteriophage M13 which is "used to display randomized peptide libraries on the surface of M13" (see middle of left column page 488) for sorting large, randomized libraries of mutants for specific proteins or peptides. The M13 is a "filamentous bacteriophage" having molecular weight of $1.9x10^6$ dalton as evidenced by Hondel et al. (see top of left column, page 55)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to apply a solution containing M13 bacteriophage virus to the membrane type includes Sartobind IDA (iminodiacetic acid) Cu^{2+} metal chelate for viral

purification, because the metal chelate affinity membrane of Sartobind have "affinity to His, Cys, Trp present in almost every protein" (see page 5 of Fischer-Fruhholz) wherein the M13 phage has been used to display expresses a protein of interest on the surface of the M13 bacteriophage with reasonable expectation of success. It would have been also obvious to one of ordinary skill in the art at the time the invention was made to apply a solution containing M13 bacteriophage displaying protein on the surface to an additional ion exchange or filtration as taught by Sartobind® Membrane Adsorbers brochure by Hirai et al. (see method of using Sartobind S100 cation exchanger, in the middle of left column) because additional purification step results in more pure product after purification.

One would have been motivated to do so because Sartorius teach the "application of Sartobind Membrane Adsorbers is advantageous especially in purification and removal of viruses for biopharmaceutical process" (see Sartobind® Membrane Adsorbers brochure by Hirai et al., Summary at the end). All physical characteristics of the Sartobind Membrane Adsorbers are already described above, which meets the limitation of Claims 9-12. Fischer-Fruhholz also disclose the Sartobind® Membrane Adsorbers is used for "Clearance of endotoxin" (see page 23), which meets the limitation of method in claim 14. Thus, the invention taken as a whole is *prima facie* obvious.

Conclusion

11. Claims 1, 4-7 and 9-15 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered section in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEXANDER D. KIM whose telephone number is (571)272-5266. The examiner can normally be reached on 11AM-7:30PM.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Bragdon can be reached on (571) 272-0931. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Alexander D Kim/
Examiner, Art Unit 1656

/Richard G Hutson/
Primary Examiner, Art Unit 1652